DETAILED ACTION

Response to Amendment and Argument

1. Claims 1-6, 9-26 and 28-32 are pending.

Claims 3-6, 13-18 and 22-24, drawn to non-elected inventions are withdrawn from examination.

Claims 31 and 32 have been added.

Claims 1, 2, 19-21 and 28-30 have been amended.

Claims 1, 2, 9-12, 19-21, 25, 26 and 28-32 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Grounds of Rejection

Claim Rejections - 35 USC § 102

3. The rejection of claims 1, 2, 9-12, 19-21, 25, 26 and 30 under 35 U.S.C. 102(e) as being anticipated by Afar et al./ U.S. Patent Application Publication number US 2003/0232350 A1 (filed November 13, 2002) is withdrawn in light of Applicants' amendment to independent claims 1, 19 and 20.

New Grounds and Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***THIS IS A NEW MATTER REJECTION***.

Applicants have added two new claims, claims 31 and 32 and allege support for these claims "...can be found at least at page 79, fourth paragraph and Figure 14", see Remarks submitted May 5, 2011, page 7, "New Claims" section. The Examiner has reviewed these particular sections of the specification, as well as others and does not find support for the two newly added claims.

Claim 31 reads,

> *"A method for detecting gastric cancer, comprising:*
> *(a) providing a sample from said patient; and*
> *(b) detecting over-expression of a cystatin SN ("CST1 ") protein having a molecular weight higher than that found in subjects not having gastric cancer."*

Figure 14 depicts Western analysis of markers in tumor and non-malignant tissue, however it is not clear from what type of tissue this assay is based. It is not clear if this gastric tissue, breast

tissue or lung tissue. Moreover, it is not clear what the molecular weight is of the expressed products shown on Figure 14 and corresponding caption listed on page 79, lines 15-18. Protein expression noted in Figure 14 is not the same as molecular weight, hence for the reasons cited herein, claim 31 is not supported by the specification.

Claim 32 reads,

> *"The method of Claim 31, where said molecular weight of said CST1 in said patient is about 35 kD, about 45 kD, or about 65 kD."*

Once again the specification seems not to support the new claim, claim 32. Page 79 of the specification, lines 19 and 20 lists three major bands, ***34***, 45 and 65kDa. While the claim does note "about 35 kD" this not the same as what is listed in the specification. Applicants should delete the new matter or clearly set forth where in the specification support can be found.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The rejection of claims 1, 2, 9-12, 19-21, 25, 26, 28-30 and new claims 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over Afar et al./ U.S. Patent Application Publication number US 003/0232350 A1 (filed November 13, 2002), and further in view of Mack et al./ U.S. Patent Application Publication number US 2004/0076955 A1 (filed July 2, 2002) and Clarke et

al./ U.S. Patent Application Publication number US 2006/0019256 A1 (effective filing date June 9, 2003) is maintained.

Applicants assert "...the combination of [references] do not teach using a specific combination of CST1, SERPINH1 and INHBA to detect gastric cancer", see page 8 of Remarks submitted May 5, 2011. Applicants request the rejection be withdrawn and the claims allowed. These points of view have been carefully considered, but found unpersuasive.

The primary reference, Afar does not fall. Afar teaches a method of immunodiagnosing stomach cancer comprising identifying and comparing diagnostic markers, including cystatin SN (SEQ ID NO: 108) and a host of others in biological samples including blood, see page 14, section 0096; page 36, line 60; page 88, line 33; the sequence alignment has been provided previously; page 10, section 0067; and page 19, section 0158. The diagnostic markers are detected in biological samples include blood, plasma, serum and stool, see page 14, section 0096. Afar teaches sequences that are up-regulated in cancer including CST1, see page 10, section 0064 and 0067. Absent evidence to the contrary the CST1 taught in Afar is the same as listed in the claims and intrinsically will have the same characteristics, i.e. molecular weight. Afar does not teach measuring overexpression of markers, serum proteinase inhibitor, Clade H (heat shock protein 47) member 1 (collagen binding protein 1) (SERPINH1) and inhibin beta A (INHBA) set forth in the newly amended claims 1, 19 and 20.

However, Mack teaches a method of diagnosing several solid cancers comprising identifying and comparing diagnostic markers listed in Tables 1A-13 including cystatin SN in many types of samples using diagnostic assays, see page 2, sections 0026-0030; page 3, section

0054; page 11, section 0108; page 21, section 0209; page 108, Table 4a; and page 112, Table 6A, Pkey number 409757. Examples of additional diagnostic markers to be assessed are olfactomedin, (OLFM1), page 35; SPARC-like 1, page 36; matrix metalloproteinase 12 (MMP12), inhibin (INHBA), pages 45, 55 and 58; lysyl oxidase, page 54; lumican (LUM), page 126; thrombospondin 2 (THBS2), page 134; TGFB inducible early growth response (page 9A); kallikrein 11 (page 150); aldican (page 154); and chondroitin sulfate proteoglycan 2 (page 167). Moreover, Clark teaches characterizing and diagnosing cancer by assessing several markers, serine or cysteine proteinase inhibitor clade B (SERPINB5), secreted acidic cysteine-rich protein (SPARC) see page 12, lines 2 and the 25th line from the bottom of the page and serine or cysteine proteinase inhibitor clade H (SERPINH1), see page 13, line 16. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include these cancer markers designated in Mack and Clarke for gastric cancer diagnosis. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary references teach these markers' upregulated expression is consistent with solid tumors, such as gastrointestinal cancer, see Clarke page 5, section 0050. Consequently, the rejection is maintained.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana Harris Dent, Ph.D. whose telephone number is (571)272-0831. The Examiner can normally be reached on 8 am to 8 pm, Monday through Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris Dent, Ph.D.
13 July 2011
/Alana Harris Dent, Ph.D./
Primary Examiner, Art Unit 1643